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OF THE CHILDRENS HOSPITAL

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THE EDITOR.

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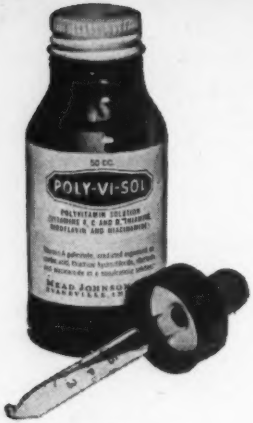

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DUPLICATION OF THE ALIMENTARY TRACT

Case Report No. 191

Joseph M. LoPresti, M.D.
Paul Kaufman, M.D.
Harold H. Hawfield, M.D.

C. A. H. 50–5109

This seventeen day old white female infant was admitted to Children's Hospital on April 23, 1950 with a history of repeated and frequent vomiting. She was the product of a normal spontaneous delivery on April 6, 1950 and weighed six pounds, eleven ounces at birth. The patient did well in the hospital immediately after delivery and was discharged at the age of one week. On arriving home she began to spit up formula occasionally. Four days prior to admission, the infant began to vomit shortly after every other feeding. This vomiting was projectile in character. The bowel movements had been frequent, usually one after or during each feeding, yellow in color and very soft. The weight on admission was seven pounds.

Physical examination revealed a well developed and well nourished white infant. The state of hydration appeared to be good with normal tissue turgor. On physical examination it was noted that shortly after taking about two ounces of formula the baby would vomit projectily and the vomitus was bile-stained. No peristaltic waves could be observed. The remainder of the physical examination was normal. The liver was palpable 2 centimeters below the right costal margin. No masses could be palpated. The impression on admission was pylorus spasm with other types of obstruction to be ruled out.

The accessory clinical findings revealed the hemoglobin to be 17.5 grams; the red blood cells, 5,000,000; white blood cells, 8,500 with 52 polymorphonuclears per 100 cells (42 segmented cells, 8 staphs, and 2 juvenile forms), 45 lymphocytes, and 3 eosinophiles per 100 cells. The platelets were normal. The urine was entirely negative. The patient was followed closely in the hospital and examined daily for possible changes in her physical findings.

On April 28, 1950 or five days after admission, a definite mass was palpable in the right side of the abdomen just lateral to the umbilicus. The mass was described as 3 centimeters in diameter, firm and freely movable. A flat plate of the abdomen revealed nothing remarkable. On May 1, a flat plate of the abdomen revealed a mass 4½ centimeters in diameter in the right flank below the liver which displaced the intestines to the left. Intravenous pyelogram done at this time revealed the calyces of the right kidney to be fairly well outlined with apparently an upward displacement by the mass. The left kidney was never satisfactorily visualized. On May 2, a barium enema revealed the mass to lie anterior to the ascending colon with no evidence of intrinsic or extrinsic obstruction. Repeat hemogram revealed a hemoglobin of 13.5 grams; red blood cells 4,300,000; white blood cells, 9,500; with 53 polymorphonuclears, 46 lymphocytes, and 1 eosinophile per 100 cells. The urinalysis was essentially normal.

On May 5, twelve days after hospitalization, the patient was explored for a right abdominal tumor. A right subcostal incision was made and the peritoneal cavity was entered. The stomach and pylorus were apparently normal. On exploration of the remainder of the abdomen, a very freely movable tumor in the right lower quadrant was palpable and was delivered into the incision. The tumor involved the terminal

portion of the ileum at the ileocecal valve. The cecal wall was very thin and the cecum was collapsible. The terminal portion of the ileum was edematous and its wall was markedly thickened. The intestinal tumor in the ileal wall was approximately 3 to 4 centimeters in size and was quite firm and appeared to be white. A wedge resection of the terminal ileum and ascending colon was carried out and an end-to-end anastomosis on an oblique angle was performed. The mesenteric defect was closed and the wound approximated in layers without drains.

Post-operatively, the patient was placed on intravenous aureomycin, 50 milligrams every 6 hours, in a continuous intravenous drip. Local phlebitis due to intravenous aureomycin appeared on one occasion in the scalp veins. At this time the leukocytes numbered 20,900 with 73 per cent polymorphonuclear forms.

Frequent vomiting persisted and it was decided that the patient had either peritonitis or further obstruction. On the third post-operative day, the initial right subcostal incision was reopened and a slight amount of cloudy fluid was encountered. On exploration of the ileocecal region at the site of the former end-to-end anastomosis, the ileum and ascending colon were adherent to the parietal peritoneum. On freeing this adhesion a leakage occurred at the site of the end-to-end anastomosis. This leakage and a sluffing of the suture line had apparently sealed off and had become adherent to the parietal peritoneum and thus prevented generalized peritonitis. In so doing, an angulation of the bowel due to adhesions had caused an obstruction. At operation the area of leakage was closed and a side-to-side ileocolostomy was performed distal to the pervious end-to-end anastamosis.

Post-operatively the patient was placed on dihydro streptomycin, 125 milligrams every 6 hours and procaine penicillin 300,000 units daily. The infant was maintained on continuous intravenous fluids alternating Ringers Solution, glucose in distilled water, plasma and blood; and on May 9, or the first post-operative day, the patient was placed on one dram of glucose water every hour by mouth. At that time it was noted that the child passed a small, greenish stool. On May 10, the second post-operative day, the patient was placed on an evaporated milk formula, 1½ ounces every 2 hours. On May 12, it was necessary to give the child Kaopectate because of diarrhea and the formula was continued as before. At that time she was having greenish-yellow stools. From this point, the diet was advanced by increasing the concentration of milk and adding carbohydrate according to the patient's toleration. On discharge, May 24, the child was having normal yellow stools and there was no evidence of vomiting. The abdomen was soft and the wound was well healed.

The pathology report described the tumor as 4 x 3 x 3 centimeters, embedded subserosally on the inferio-lateral wall of the cecum. On section, the tumor was cystic with a thick, firm, white wall which varied in thickness from 2 to 4 millimeters in width. A fibrous band was found running across the cyst. On microscopic examination all sections showed normal small intestine except for the mucosa. Replacing the mucosa was a thin, fibrous layer containing an abundance of capillaries and an infiltration of lymphocytes. In certain areas there was a layer of flattened cuboidal cells from 1 to 4 cells in thickness. The pathological diagnosis was intestinal duplication. A subsequent three-month follow-up of the patient revealed that the child is taking her formula well and has made a satisfactory weight gain.

DISCUSSION

Duplications of the alimentary tract have been described in the literature under various names; e.g., enteric cyst, enterogenous cyst, diverticula,

giant diverticula, ileum duplex, jejunum duplex, unusual Meckel's diverticulum, and so forth. As all of these names are used to describe the same condition, though occurring in different situations, it would seem desirable to apply one common name.

This anomalous condition is rare. A review of the admissions to this hospital in the past ten years revealed only one such case (cf. Case Report). In a comprehensive review of the medical literature, the authors were able to locate 150 recorded cases (Table I). The distribution of these cases between both sexes is approximately equal. Since the anomaly is present from birth, most of the patients fall into the pediatric age group. In a few instances symptoms do not appear until adulthood, or the condition has been diagnosed coincidentally in the autopsy room.

Many theories as to the origin of duplications of the alimentary tract have been advanced. However, the experiments of Lewis and Thyng[1] explain most satisfactorily the derivation of duplications of the alimentary

TABLE I

Anatomical Distribution of 150 Reported Cases of Duplication of the Alimentary Tract

Tongue	2
Esophagus	16
Stomach	8
Small Intestine	115
Large Intestine	5
Rectum	4
Total	150

tract. These investigators found very regularly in pig, rabbit, and human embryos, nodules of epithelial cells occurring along the course of the esophagus, stomach, and intestine. These nodules become vacuolated and may be separated from, or be in continuity with the lumen of the alimentary canal. Normally, these disappear or coalesce to form a part of the lumen of the digestive tract, but they may persist. Evans' collected cases[2] support this theory of origin since some had an anatomic similarity to the embryologic structures pictured by Lewis and Thyng. The co-existence of mediastinal cysts and abdominal cysts of enteric origin is additional evidence in support of this view.

The exact nature of the pathology has been delineated only in recent years. Since the report of Poucher and Milles[3], numerous scattered reports have appeared[4, 5, 6, 7, 8, 9, 10]. The largest series of operated cases have been reviewed by Ladd and Gross[11]. Pathologically, duplications of the alimentary tract present three characteristics which are common to all of them:

1. Each has an epithelial lining similar to that of some part of the stomach, intestines, or colon, but it does not necessarily correspond to the mucosa at the level at which the duplication is found.

2. Each has a smooth muscle coat.

3. Each is contiguous with and strongly adherent to some part of the alimentary tube.

The size of the duplication varies from that of a small oval cyst to an elongated tube. In the majority of cases there is no connection between the duplication and the alimentary canal. The contents are usually serous and secreted by the lining membrane. If pressure necrosis has occurred, the fluid may be hemorrhagic.

The distribution of these lesions is of particular interest. While it is true that they may occur at any site along the digestive tract, there is a definite predilection for the small intestine, especially the ileum. Seventy-six per cent (114 cases) of the 150 cases collected from the medical literature were located in the small intestine. Of these, 76.3 per cent (88 cases) occurred in the ileum or at the ileo-cecal junction. *Approximately half of the duplications which were discovered in the mediastinum were associated with intra-abdominal duplications.* Duplications were found to be most rare in the region of the tongue (Table I).

The symptomatology depends on the location and size of the duplication. In the region of the tongue, the symptoms are those of high laryngeal obstruction. Mediastinal duplications cause symptoms by external pressure on the trachea and bronchi; e.g., cough, cyanosis, and dyspnea. When the duplication is located in the intestinal tract, there is usually a palpable mass noted. Depending on the size of the mass, partial or complete obstruction is produced. Vomiting and obstipation are common. Pain may be produced by distension of the mass by its fluid contents. The tumor may be in such a location as to interfere with the mesenteric blood supply to the intestine. When this occurs, as it often does, it produces necrosis, sloughing, and bleeding of the adjacent intestine. Hematochezia is a common finding in intestinal duplication. Of particular interest are those duplications located in the region of the duodenum. In only one case did symptoms become manifest after the age of one month. In almost every case the pre-operative diagnosis was pyloric stenosis. Projectile vomiting, intestinal patterns, constipation, weight loss, and a palpable mass were present in the majority. In the region of the rectum these lesions produce a sense of fullness, prolapse, and the presence of a palpable cystic mass between the posterior wall of the rectum and the coccyx.

Pre-operatively the diagnosis is only rarely made and x-ray examinations are of little value in establishing the diagnosis. However, the symptoma-

tology is such that surgical intervention must be resorted to in the majority of cases.

In most instances, the treatment of choice is resection of the duplication and its adjacent gut, and then reestablishment of intestinal continuity by a side-to-side anastomosis. In a few cases it may be necessary to open the cyst, and resect a portion of it and the remainder marsupialized to the anterior abdominal wall. The structure may then be packed with gauze to destroy its lining membrane. Some days after operation, the packing may be withdrawn, allowing the cyst walls to fall together and coalesce. With early and careful surgical intervention, adequate post-operative care, and effective antibiotic therapy, the future outlook of these patients is good.

SUMMARY

1. A case of duplication of the small intestines has been presented.
2. A discussion with a review of the medical literature of this interesting pathological entity has been attempted.

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METHYL SALICYLATE POISONING

Case Report No. 192

Hobart T. Feldman, M.D. C. L. S. 50-8340

This report represents the only case of methyl salicylate poisoning admitted to Children's Hospital within the past eighteen months. The majority of previous admissions recovered after a stormy hospital course.

CASE REPORT

C. L. S., a twenty month old white female was admitted to the hospital on July 11, 1950. The patient had been well until the morning of admission when she accidentally drank 1 ounce of methyl salicylate. One-half hour later she was given crackers and milk and vomited. The vomitus had the odor of oil of wintergreen. This therapy was repeated twice within the next one and one-half hours with similar results. Three hours after ingestion, the child became listless. She was brought to the hospital where stomach lavage was performed, following which she was hospitalized.

Physical examination revealed a stuperous, semi-conscious, white female lying listlessly in bed with arms and legs outstretched and flaccid. Her eyes occasionally rolled upward and an intermittent lateral and vertical nystagmus was noted. Respirations were 48 per minute, deep and regular. The pulse rate was 160 per minute. The heart sounds were of fairly good quality. The blood pressure was 108/56. There was generalized areflexia present. The skin was warm and dry and no rash was evident. The buccal mucosa and pharynx appeared normal.

Immediately after admission, blood was withdrawn for a carbon dioxide combining power, and an intravenous infusion of 5 per cent dextrose in normal saline was started. The carbon dioxide combining power was reported as 28 volumes per cent. The intravenous administration of saline was discontinued, and replaced by 150 milliliters of 1/6 molar lactate. The patient became comatose within an hour after admission. One hundred-fifty milliliters of 10 per cent dextrose in water, with an equal amount of isotonic Ringers solution was given by hypodermoclysis. Three hours after admission, the carbon dioxide combining power was 29 volumes per cent and 200 milliliters of 1/6 molar lactate was given intravenously. The prothrombin time was 40 per cent of normal. A complete blood count revealed 11.5 grams of hemoglobin; 4,500,000 red blood cells, 13,300 white blood cells, with 75 per cent neutrophiles (with many toxic granules) and 25 per cent lymphocytes. The blood salicylate level was 43 milligrams per cent.

Within three and one-half hours after admission the patient began to show clonic, convulsive movements of the extremities, which were temporarily controlled by the hypodermic injection of ½ grain of sodium phenobarbitol. The child progressed rapidly into deep coma and shock. A phlebotomy was performed and plasma was injected under pressure. In spite of these measures plus the administration of caffeine sodium benzoate and artificial respiration, the patient expired that night approximately eight hours after admission.

An autopsy revealed only congestion of the abdominal viscera.

DISCUSSION

Samuel P. Bessman, M.D.: This patient's symptoms are typical of salicylate intoxication, a syndrome which suggests itself even at physical examination. The picture of a patient who is semistuperous with hyperventilation, yet no dehydration such as accompanies other forms of acidosis, e.g. diabetic coma or diarrhea, is characteristic of salicylism. There are, of course, other causes for hyperpnea of the acidotic type, but the most common etiology for the concurrent symptoms of hyperpyrexia, hyperpnea, and stupor without dehydration is salicylism. In addition to the picture presented by salicylism per se, we have the further complication produced by the methyl ester of salicylic acid which is hydrolyzed immediately to methyl alcohol. This adds methanol intoxication to the biochemical problems caused by salicylate.

Now a word about the pathogenesis of salicylate intoxication. The exact chemical reactions involved have not as yet been elucidated, but objective evidence that there is an initial "stimulation" of respiration has been observed by many workers. The site of action is obscure. Following the initial hyperventilation which lasts for from four to twelve hours with resulting increase in serum pH together with a minor diminution in serum bicarbonate, i.e., respiratory alkalosis, a true acidemia ensues with production of acetone, beta hydroxybuteric acid and aceto-acetic acid. This acidemia has been described as "intractable" because it is not correctable immediately with what may seem to be adequate quantities of bicarbonate-producing solutions such as 1/6 molar lactate. This has been ascribed to a failure of lactate metabolism but is more likely due to the fact that there is a continuing intoxication of the carbohydrate oxidizing mechanism resulting in a utilization of fat and a picture remarkably similar to diabetic acidosis.

The effect of salicylate on many enzyme systems has been studied and it has been shown that glycogen deposition in the liver is markedly affected by feeding salicylate to experimental animals. Further, the oxygen utilization by the liver has been shown to be diminished significantly in the presence of amounts of salicylate corresponding to toxic levels in the blood. Interesting subjective evidence concerning a chemical activity of salicylate which might lead to this impairment of carbohydrate metabolism is furnished by the observation of Link and his co-workers that the structure of salicylates is similar to the structure of dicumarol. This brings us to another outstanding symptom of salicylate intoxication and that is the hemorrhagic tendency. This tendency is due to the lowering of blood prothrombin which is exactly the same as that caused by dicumarol. The lowering of blood prothrombin appears quite early in the course of salicylate intoxication and was demonstrated by this patient within the first twenty-four hours. It

was postulated on the basis of Link's observation that dicumarol exerted its action by becoming salicylate. The difficulty with this assumption is that it requires about eight times as much salicylate to produce the same drop in prothrombin as a single dose of dicumarol. Thus, the possibility suggests itself that the reaction goes actually in the *opposite* direction and that salicylate reacts in the body to form a dicumarol-like substance which acts on the prothrombin production by the liver in a manner similar to dicumarol. If we look for a moment at the possible significance of such a reaction, we see that a 5-carbon chain compound with an acid group at each end could react with 2 molecules of salicylate to form dicumarol by reactions known to occur in the body with other substances. This 5-carbon compound actually is present in the body and is, interestingly enough, an essential member of the oxidative carbohydrate cycle, viz., alpha ketoglutaric acid. This carbohydrate cycle (Krebs cycle) is the pathway by which the major part of protein and fat and all of carbohydrate oxidation occurs. Thus, if it were interrupted through the removal of one of its essential components, symptoms referable to *oxidative* defects of metabolism would be caused. If we compare the symptoms of salicylism to those of diseases with a known impairment of exudative metabolism we find a striking similarity among all of them, e.g., carbon monoxide poisoning, cyanide poisoning, high altitude sickness, and asphyxia.

The pathological picture in the brain resulting from salicylate intoxication is the same as that resulting from anoxic anoxia. The fact that the symptoms of salicylate intoxication appear to be confined to the brain takes our attention from the possibility that a general metabolic poisoning may actually be the problem. The reason for this apparent localization of symptoms to the brain is that the brain metabolism is based solely on carbohydrate oxidation and, therefore, any impairment of carbohydrate oxidation in general would manifest itself first in cerebral symptoms. The reason for the apparent intractability of the acidemia of salicylate intoxication is that the salicylate requires quite a long time for excretion and there is no mechanism known at present whereby we can counteract the effect of this intoxication. In diabetic coma, we are in a much better position to treat a similar metabolic difficulty because we can furnish the patient with insulin, the lack of which is the cause of the symptoms. No such mechanism can be called into action in salicylism.

A logical approach to therapy would be four-fold:

1. Observe whether a prothrombin deficiency develops by taking frequent prothrombin determinations. At the first sign of falling prothrombin rate, administer a rapid-acting vitamin K substance, such as K_1 oxide, and then administer plasma.

2. Treat the difficulty in carbohydrate metabolism as best we can at the

present time by the administration of adequate amounts of glucose in order to preserve and to store liver glycogen which has been shown to be diminished in salicylate intoxication.

3. Follow the blood carbon dioxide content and pH, and administer sodium lactate in adequate amounts to bring the carbon dioxide content of the blood to approximately normal. This can be done by administering a single dose of lactate calculated by Hartmann's (30 milliliters 1/6 molar lactate per kilogram equals a rise of 16.6 volumes per cent carbon dioxide) or any other formula. Measure the carbon dioxide content of the blood five or six hours later to note the effect of therapy. If the carbon dioxide content has not risen, a further dose of lactate is indicated with subsequent checks on the carbon dioxide content until the carbon dioxide content of the blood *remains* at a normal level.

4. Stimulate the elimination of salicylate from the body. The administration of the large quantities of lactate necessary to correct the acidemia which eventually develops in all cases of severe salicylate intoxication aids in the elimination of salicylate. It has been shown by several workers that alkali administration with any organic acid radical such as salicylate, stimulates its renal excretion. If only small amounts of lactate are required for the acidemia then mild alkali and electrolyte must be administered in the form of Hartmann's solution to stimulate the elimination of salicylate.

In this case we are dealing with not only salicylism but also methyl ester intoxication which is much more fatal and incapacitating than salicylate, and the majority of deaths in salicylate intoxication are caused by ingestion of methyl salicylate. There are several reasons for this, among which are: the marked toxicity of the methyl salicylate and the liquid nature of the compounds containing methyl salicylate. Apparently, the sweet-smelling oil of wintergreen is much more attractive than aspirin pills to children, and secondly, the liquid is much more easily swallowed in toxic doses than are the relatively distasteful pills which must be chewed to be consumed. The treatment of methyl alcohol intoxication is similar to the treatment outlined for salicylate intoxication and no alterations are necessary in the regime if either aspirin or oil of wintergreen has been ingested.

CLINICO-PATHOLOGICAL CONFERENCE

Directed by: E. Clarence Rice, M.D.
Assisted by: Richard J. Waters, M.D.
By Invitation: Hobart T. Feldman, M.D.

Richard J. Waters, M.D.

G. S., a four months old colored male, was admitted to Children's Hospital on October 1, 1949 and died on October 17, 1949.

History reveals that the baby had been considered well until the day prior to admission at which time he developed fever, vomited all feedings, and had five brown semi-solid stools. He was brought to the out-patient department where weak tea was prescribed and a blood count was taken. The symptoms continued, and on return visit the following day, the infant was admitted for treatment and observation because of a severe anemia.

Past history reveals that this patient was the second born of premature twins of seven months' gestation. These infants weighed 1 pound 9 ounces and 2 pounds respectively at birth. The first twin died of pulmonary atelectasis after seven hours. The patient was kept at Freedman's Hospital for two months and was discharged weighing 5 pounds. He was doing well on an evaporated milk formula and pureed foods at home, and had not been seen by a physician.

On admission, the patient's temperature was 102.0 F. Physical examination revealed a fairly well nourished but underdeveloped colored male infant weighing 10 pounds with slight peri-orbital edema. The significant findings included dehydration with loss of skin turgor and marked palor of conjunctivae and mucous membranes.

During the first three hospital days the patient's temperature varied from 99.0 F to 101.0 F and thereafter was normal. Initial hemogram revealed 2,000,000 erythrocytes and 5.5 grams of hemoglobin. On October 2 the child was transfused with 100 milliliters of whole blood. The following day he had six loose brown stools and appeared anemic and dehydrated. On October 4 marked pallor and edema of the scrotum and lower extremities was noted. At this time abdominal palpation revealed a large, firm mass in each flank. Urinalysis showed gross hematuria which persisted throughout the remainder of his hospital stay. A flat plate of the abdomen taken at this time was read by the roentgenologist as "hepatosplenomegaly with displacement of the large and small gas-distended bowel forward and toward the midline by bilateral flank masses." Pallor persisted and the hemoglobin dropped to 3.2 grams. The patient was again transfused. Dyspnea developed on October 6, and oxygen was started and continued. On October 7 bright red blood was noted in the stools, and for the remainder of the patient's hospital stay the stools were black, semi-solid, small in volume, and occurred two to three times daily. Dependent edema progressed, and the patient retained very little by mouth. Fluid and electrolyte intake was maintained by intravenous infusions and clyses. Despite adequate intake of fluid, the patient became anuric on the fourteenth hospital day and remained so until his demise four days later. On October 17 he developed severe dyspnea, cyanosis and clonic convulsive episodes. Despite oxygen therapy, aspiration, and stimulants, he expired.

Treatment while in the hospital consisted of blood transfusions, parenteral fluids, oxygen, penicillin, and other supportive measures.

Significant laboratory data included:

1. Hemograms: erythrocytes, 1,000,000 to 2,500,000
   hemoglobin, 3.2 grams to 8.0 grams
   leukocytes, 15,000 to 30,000 with 60–80 per cent polymorphonuclears.
2. Bone marrow: "Decreased megakaryocytes, otherwise normal."
3. Sickling Preparation: negative.
4. Coombs Test and abnormal A or B agglutinins: negative.
5. Fragility

	Patient's cells	*Control*
Hemolysis begins	0.38 per cent	0.46 per cent
Hemolysis complete	0.28 per cent	0.34 per cent.

6. Kahn and Mazzini: negative.
7. Prothrombin: 108 per cent of normal.
8. Urinalyses: gross or microscopic blood in all specimens;
   Albumin—10 to 400 milligrams per 100 cubic centimeters.
9. Non-protein nitrogen: October 4, 42 milligrams per 100 cubic centimeters
   October 12, 148 milligrams per 100 cubic centimeters
   October 14, 123 milligrams per 100 cubic centimeters
   October 16, 126 milligrams per 100 cubic centimeters.
10. Total proteins: 4.94 grams per 100 cubic centimeters
    Albumin: 3.92 grams per 100 cubic centimeters
    Globulin: 1.02 grams per 100 cubic centimeters.
11. Stool culture: no growth.

DISCUSSION

Hobart T. Feldman, M.D.: This infant had done very well from his birth up to the onset of the acute episode which terminated fatally. The remarkable increase in weight from 2 pounds at birth (after a seven month gestation) to 10 pounds at the time of his admission seems to offer conclusive evidence that he was in exceptionally good health prior to his illness.

The finding of a "severe anemia" on the day of admission, in a previously well child, points to some sort of vascular accident with hemorrhage. Since there was no evidence of external bleeding, this must have occurred within one of the body cavities, most likely within the abdomen. The dehydration evident on admission could be accounted for by persistent vomiting of one day's duration, although we have all seen infants with a history of vomiting for several days who are remarkably well-hydrated. Such dehydration would not have been the result of loss of fluids via the large intestine, because the stools were described as semi-solid, five within twenty-four hours. Many normal infants have five semi-solid stools a day.

The uremic death after seventeen days in the hospital in spite of transfusions, the attempts at hydration, the use of oxygen, the penicillin administration, plus the other supportive measures suggests gross abnormality of the kidneys or the urinary tract. This abnormality could be either primary in origin or secondary to pathological changes elsewhere. The large,

firm mass in each flank was the outstanding physical finding, and was apparently the cause of rapid, progressive renal failure evidenced by hematuria, albuminuria, and elevation of the plasma non-protein nitrogen.

I would like to approach this diagnostic problem by evaluating *the causes of abdominal masses in children.*

I. Enlargement of the kidneys, or enlargements in the kidney regions, which can result in azotemia:
   1. Congenital polycystic disease
   2. Obstruction below the kidney with hydronephrosis
   3. Wilm's tumor
   4. Neuroblastoma, neurofibroma, hemangio-endothelioma, etc.
   5. Tuberculosis
   6. Retroperitoneal hemorrhage
   7. Lipoid nephrosis.

II. Hepatosplenomegaly:
   1. Primary neoplasm and metastatic lesions
   2. Cirrhosis
   3. Congestive heart failure
   4. Hepatitis
   5. Banti's disease
   6. Glycogen storage disease
   7. Tuberculosis
   8. Malaria
   9. Cooley's anemia
   10. Leukemia.

Congenital Polycystic Kidneys: This condition is frequently bilateral, and may or may not cause renal failure, depending upon the size of the cysts. The sudden onset of this infant's illness and his previous well-being make the possibility of this condition unlikely. Intravenous pyelography at this age would have offered little if any diagnostic assistance.

Obstruction below the Kidney with Hydronephrosis: This does not usually involve both kidneys. A mass in or around the urinary bladder resulting in bilateral ureteral obstruction would have presented a more chronic course. There was no palpable mass, nor x-ray evidence of a tumor in this region.

Wilm's Tumor: This has been reported in infants and children from two months to nine years of age. It is rarely bilateral, and metastasizes to the lungs and then to the brain. I do not consider this a likely possibility in this case.

Neuroblastoma: A mass in the abdomen with diarrhea and fever obligates one to consider neuroblastoma. Early metastases in the liver, orbit, and skeleton are characteristic; no metastatic lesions were seen in this case.

Acute Miliary Tuberculosis with hepatosplenomegaly may occur at any

ago and the tuberculin reaction may be negative early. The presence of abdominal masses within twenty-four hours after the onset of this patient's illness renders such a possibility unlikely.

Retroperitoneal Hemorrhage: The fever, hematuria, anemia, and lack of response to treatment in this infant make this entity a good possibility, and could account for the bilateral abdominal masses and renal failure.

Hepatosplenomegaly: This may be the result of primary neoplasm, cirrhosis, congestive heart failure, hepatitis, Banti's disease, malaria, Cooley's anemia, syphilis, tumors of the lymphomata group, or leukemia. These diseases are mentioned only because the masses in the abdomen, demonstrable by x-ray, were described as "hepatosplenomegaly." The clinical picture and the laboratory findings do not corroborate these possibilities.

Several types of anemia must be considered in evaluating the possible cause of this infant's illness. Cooley's anemia is characterized by enlargement of the liver and spleen but the typical basophilic stippling, Howell-Jowell bodies, Cabot rings, target cells, nucleated red blood cells, and bone changes were not evident in this patient.

Congenital Hemolytic Anemia: This entity is infrequently seen in infants, and clinical manifestations are relatively rare in infants under one year although severe hemolytic crises have been reported. Increased erythrocyte fragility, spherocytes, reticulocytes, and jaundice were not present in this patient.

Sickle Cell Anemia: This disease is excluded as a possibility by the absence of sickling and the typically widened erythrocyte fragility span.

Idiopathic Fulminating Purpura Hemorrhagica: This entity may prove fatal in the first attack, and internal bleeding into the retroperitoneal or renal areas could have accounted for this patient's fatal course; however, there was no apparent evidence of petechial hemorrhages and ecchymoses in the skin and mucous membranes. Unfortunately, the coagulation and bleeding time and the platelet count of the peripheral blood were not determined. It seems to me that these simple procedures are extremely important facets in any hematological investigation, and should be determined before one undertakes a bone marrow biopsy.

Acute Leukemia, *Lymphoblastoma* or *Lymphosarcoma* are accompanied by the presence of primitive or other abnormal cells in the peripheral blood or bone marrow, none of which were evident in this patient.

In reviewing this infant's history and his course after admission to the hospital, I am impressed by the following points:

1. A sudden onset of fever, vomiting and severe anemia in a four month old colored male whose previous development had been excellent;
2. Three days after admission the onset of scrotal and lower extremity edema which was progressive;
3. The presence of a large, firm mass in each flank;

4. The failure of the anemia to respond to several blood transfusions;
5. Rapidly progressive azotemia with hematuria and albuminuria; and
6. Anuria.

I am of the opinion that this infant's death was caused by a retroperitoneal hemorrhage into the kidneys or into the peri-renal areas resulting in lower extremity edema due to obstruction of the venous return from the legs and a rapid loss of renal function.

PATHOLOGIC DISCUSSION

E. Clarence Rice, M.D.: The body was that of a well developed colored male, weighing 4,479 grams; and 53 centimeters in length (normal 61 centimeters). The birth had been premature after a seven months' gestation. No icterus was observed. The abdomen was markedly protuberant. While generalized edema was noted, that of the scrotum and penis was especially marked.

The significant findings were noted in the brain, the kidneys, renal veins, and inferior vena cava.

The brain weighed 492 grams (normal 644 grams). An excessive amount of fluid was present in the subarachnoid space. The rolandic veins of the right hemisphere were thrombosed to a point midway in the parietal lobe. The left rolandic veins were thrombosed to the Sylvian fissure and several thrombosed veins were observed to enter the longitudinal sinus. The frontal gyri were irregular and microgyric. Sections of the brain demonstrated a hemorrhage in the right post-parietal lobe measuring 7 by 3 by 3 millimeters in the white matter adjacent to the middle gyrus. Another small hemorrhage in the right middle parietal lobe adjacent to the superior gyrus was also present.

Each kidney weighed 100 grams, the normal being 25 grams; each measured 5 by 8 centimeters. Both were enlarged to approximately four times their normal size. Fetal lobulation was retained. The right kidney externally showed evidence of hemorrhage and both had a greenish appearance. The renal arteries and the aorta were normal. The inferior vena cava was thrombosed distal to the liver; the thrombosis involved the renal veins and extended up into the kidney parenchyma with infarction. The capsule was thickened and when removed showed evidence of subcapsular inflammatory reaction. The sectioned tissue revealed poor differentiation between cortex and medullae, the parenchyma having a rather bright red appearance.

Microscopic examination of the kidneys showed variable degrees of necrosis most marked in the region of the pelves which were the sites of old and recent hemorrhage. Vague outlines of collecting tubules and thrombosed vessels were present. Leukocytic invasion of the thrombi and renal parenchyma were noted. Several tubules were calcified. Numerous bacilli

were seen in these areas. In the cortex, remnants of glomeruli and tubules were seen and numerous leukocytes were present in the disintegrating tissue. Near the periphery of the kidneys the structures were more distinct, and hemorrhagic glomeruli were observed. Occasionally a few areas having undergone little change were noted. One large area beneath the capsule was the site of a heavy infiltration of leukocytes being representative of an abscess; the adjacent tissue was compressed. The renal vein was the site of an organizing thrombus.

Escherichia coli was obtained by culture of the cisternal fluid and kidneys, and *Proteus morganii genus paracolon* was obtained from the heart's blood.

Pathological Diagnosis:

1. Bilateral renal infarction
   Thrombosis of renal veins and inferior vena cava
2. Thrombosis of meningeal veins
3. Cerebral hemorrhage
4. Pulmonary edema and emphysema
5. Congestion of abdominal viscera.

Although similar findings have been reported by various observers, infarction of the kidneys due to thrombosis of the renal veins and vena cava has not been seen with any frequency by the members of the Department of Pathology.

Just what were the sequences of events leading up to the patient's death? Obviously the patient was not in good health prior to his admission considering the erythrocyte count of 2,000,000 and the hemoglobin of 5.5 grams. Dehydration and diarrhea probably caused some hemoconcentration which was changed by hydration with further reduction of the hemoglobin to 3.2 grams. Was the primary pathology in the kidney manifesting itself as a pyelonephritis with thrombosis of the renal veins and extending to the vena cava; or was the thrombosis of the inferior vena cava the result of dehydration, diarrhea, venous stasis and secondary infection resulting in extension of the thrombus to involve the renal veins (presuming also, a similar vascular stasis secondary to dehydration and infection was also responsible for the cerebral vascular pathology)? We have found thrombosis of the longitudinal sinus secondary to diarrhea and dehydration in several babies who came to necropsy. It seems unlikely that the thrombosis started in the veins of the legs and extended upward above the renal veins. I am inclined to believe that the initial lesion was in the kidneys as evidenced by the marked accumulation of leukocytes in some areas and that a thrombophlebitis involving the renal veins was set up which eventually extended to the inferior vena cava. It is my impression that the cerebral vascular pathology came about as a result of the dehydration, vascular stasis and infection.

The urinalyses were typical of the findings one would expect from such renal damage and the rising leukocyte count and non-protein nitrogen are to be looked for when infection is present and renal function is seriously impaired. Uremia was apparently a terminal event.

The presence of edema restricted to the lower portion of the trunk and the legs and the finding of bilateral abdominal masses in each flank together with significant urinary findings should make one strongly suspect renal pathology on the basis of vascular obstruction.

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